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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/065,856	11/26/2002	Ann E. Loraine	3291.3A	3379

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EXAMINER

MILLER, MARINA I

ART UNIT PAPER NUMBER

1631

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/065,856

Applicant(s)

LORAIN ET AL.

Examiner

Marina Miller

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 11-21, 24, 25, 28-37, 40, 41 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 11-21, 24, 25, 28-37, 40, 41 and 43-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 August 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. <u>1 copy</u> . |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____. |

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Art Unit: 1631

DETAILED ACTION

Applicants' submission filed on 8/08/2005 is acknowledged. Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 are pending. Claims 6, 8-10, 22-23, 26-27, 38-39, and 42 are cancelled. Claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

Priority

Applicant's claim for priority under 35 U.S.C. 119(e), 120, and 122 is acknowledged. However, the applications for which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-5, 7, 11-21, 24-25, 28-37, 40-41, and 43-45 of the instant application, as set forth in the previous office action mailed 2/11/2005.

As support for the elected claims is not found in the priority applications, priority for the elected claims is granted only to the filing date of the instant application of 11/26/2002.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3-5, 7, 11-21, 24-25, 28-37, and 43-45 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Art Unit: 1631

Claims 1, 3-5, 7, 11-21, 24-25, 28-37, and 43-45 were rejected under 35 U.S.C. 101 in the previous office action mailed 2/11/2005 for lack of patentable utility. Applicants did not address the lack of patentable utility rejection in their answer filed 8/8/2005, but instead put forward arguments intended to establish that the rejected claims are directed to statutory subject matter under 35 U.S.C. 101 (*see* page 19 of the applicants' response filed 8/8/2005). However, the examiner did not reject claims 1, 3-5, 7, 11-21, 24-25, 28-37, and 43-45 under 35 U.S.C. 101 as being directed to non-statutory subject matter. Also, the amendment filed by applicants does not, *per se*, place the rejected claims in compliance with the utility requirement under 35 U.S.C. 101. Thus, for the reasons stated in the previous office action, the rejection of claims 1, 3-5, 7, 11-21, 24-25, 28-37, and 43-45 under 35 U.S.C. 101 is maintained for lack of patentable utility.

Claim Rejections - 35 USC § 112

First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentations is "undue." These factors include, but are not limited to:

- a) The breadth of the claims;
- b) The nature of the invention;

Art Unit: 1631

- c) The state of the prior art;
- d) The level of one of ordinary skill;
- e) The level of predictability in the art;
- f) The amount of direction provided by the inventor;
- g) The existing of working examples; and
- h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

Claims 1-5, 7, 11-21, 24-25, 28-37, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a) The claims are broad because they are drawn to a generic method and a system for providing information about biological molecules. The method comprises receiving a user selection of general probe set identifiers (PSIs) and unknown intensities detected by an unknown method (*see* the rejection under 112, second paragraph) and determining by unspecified fitting PSIs and generic intensities to models of generic genomic structure generally associated with alternative splice variants ("ASV").

b) The invention is drawn to a method and a system for providing genomic information over a network.

c) Prior art analysis shows that determining alternative splice variants requires analysis of thousands of hybridization reactions, assessing huge data sets of expression profiling assays, applying sophisticated models and algorithms and is difficult by using traditional molecular biology approaches. *See*, for example, Wang, US 2002/0029113, p. 1-2; Hu, *Genome Research*, 11:1237-1245 (2001).

d) The skill of those in the art of molecular biology and bioinformatics is high.

e) Prior art shows that a great deal of uncertainty exists in the field of predicting splice variants from expression data. Prior art supports complex nature of elucidating, for example, the tissue-specific pattern of alternative splicing of tens of thousands of genes. The current knowledge of splice variants in the public database is fragmented. Algorithms for predicting splice variants are limited. *See* Hu, *Genome Research*, 11:1237-1245 (2001).

f) The specification does not provide guidance for fitting probe set identifiers and intensity values to a model of genomic structure without knowledge of fitting parameters and/or criteria. The specification further does not provide guidance for how to fit (*e.g.*, statistically, physically, *etc.*), what to fit (*i.e.*, it is not known what probe set identifiers and intensity values represent), and what model to fit (*i.e.*, a genomic structure model is not known). The specification also does not provide any disclosure that the recited “fitting” will determine ASVs.

g) The specification does not provide working examples for performing a generic method and a system for providing information about biological molecules.

h) In order to practice the claimed invention, one skilled in the art must randomly select what intensity values are to be determined and a method of determining and must guess which

Art Unit: 1631

parameters to use for fitting PSIs and intensities and what model to use for fitting. This constitutes undue experimentation.

Due to the undue experimentation required to obtain the goal of the invention, the lack of directions presented in the specification, the complex nature of the invention, and the state of the prior art, the specification fails to teach one skilled in the art how to use the claimed method for one individual at a time.

Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7, 11-21, 24-25, 28-37, and 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 43 recite the limitation “intensity values detected from each probe-set.” It is not clear whether “intensity values” are detected because each probe-set of a probe array comprises, for example, a label, or whether intensity values are those previously generated in hybridization experiments between a probe-set and a sample. It is also unclear whether each probe-set is characterized by a total intensity value, or each probe in a probe-set has its own intensity value. As the intended limitation is not clear, claims 1 and 43 are indefinite. Claim 2 depends from claim 1. Claims 44-45 depend from claim 43. Therefore, claims 2 and 44-45 are further indefinite.

Art Unit: 1631

Claims 1 and 43 recite the limitation “receiving a user selection of probe set identifiers that identify ... probe-sets ... and ... intensity values.” It is not clear whether one receives probe set identifiers and intensity values or only probe set identifiers that identify probe-sets and intensity values. As the intended limitation is not clear, claims 1-2 and 43-45 are indefinite.

Claims 1, 3, 28, and 43 recite the limitation “fitting.” It is not clear whether “fitting” is intended to be, for example, a structural fitting (*e.g.*, 3D structure-to-structure fitting, sequence alignment, *etc.*) or statistical fitting (*e.g.*, using statistical algorithms to produce the “best fit” of data to a model). As the intended limitation is not clear, claims 1, 3-5, 7, 11-21, 24-25, 28-37, and 43-45 are indefinite.

Claims 1, 3, 28, and 43 recite the limitation “a model of known genomic structure.” It is not clear what “a model of genomic structure” is intended to represent, *e.g.*, a sequence, 3D structure, haplotypes, haplotype blocks, chromosomes, alleles, *etc.* As the intended limitation is not clear, claims 1, 3-5, 7, 11-21, 24-25, 28-37, and 43-45 are indefinite.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

Art Unit: 1631

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph. D., can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
9/29/05

Marina Miller
Examiner
Art Unit 1631

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